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WILSON SONSINI GOODRICH & ROSATI			DEJONG, ERIC S	
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DATE MAILED: 01/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/645,863

Applicant(s)

HELLER ET AL.

Examiner

Eric S. DeJong

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 20 December 2004 and 30 December 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1 and 3-43 is/are pending in the application.
- 4a) Of the above claim(s) 4, 6, 11-13, 21, 32-37, 39, 40, and 43 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 3, 5, 7-10, 14-20, 22-31, 38, 41 and 42 is/are rejected.
- 7) ☒ Claim(s) 16 is/are objected to.
- 8) ☒ Claim(s) 1 and 3-43 are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. <u>3 pages</u> . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)                                   |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>10 pages</u> . | 6) <input type="checkbox"/> Other: _____.   |

## **DETAILED ACTION**

The preliminary amendment filed by applicant on 17 May 2004 comprising amendments to the Drawings and Specification of the application is acknowledged.

The preliminary amendment filed by applicant on 25 May 2004 comprising amendments to the claims of the application is acknowledged. The amended list of claims replaces all previous claims for the instant application.

### ***Election/Restrictions***

Applicant's election without traverse of the specie of phenotype G) disease diagnostic, the specie of marketing M) marketing diagnostic products along with a disposable microfluidics device, the specie of entities collecting samples N) a collaborator collects samples, specie of marker P) polypeptides, and the specie of sample preparation preceding a mass spectrometry platform X) the step of preparing samples on a microfluidics device preceding the step of using a mass spectrometry platform in a telephonic interview held on 20 December 2004 and in the reply filed 30 December 2004 is acknowledged.

Claims 4, 6, 11-13, 21, 32-37, 39, 40, and 43 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made without traverse in a telephonic interview held on 20 December 2004 and in the reply filed 30 December 2004 is acknowledged.

Art Unit: 1631

Cancellation of claim 2 is acknowledged from the response filed by applicant on 25 May 2004.

Claims 1, 3, 5, 7-10, 14-20, 22-31, 38, 41, and 42 are currently under examination.

### ***Claim Objections***

Claim 16 objected to under 37 CFR 1.75 as being a substantial duplicate of claim 15. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

### ***New Matter / Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 5, 7-10, 14-20, 22-31, 38, 41, and 42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Step d) of amended claim 1 recites “marketing diagnostic products that use said representative patterns to identify said phenotypic state with a disposable device.” The original wording of claim 1 was “marketing diagnostic products using said representative patterns”, wherein said representative patterns refer to patterns of markers identified from mass spectrometry data. The diagnostic products marketed were originally limited only by using “said representative patterns”. Instant claim 1 now reads on the limitations that the diagnostic products being marketed use “said representative patterns” and the specific application “to identify said phenotypic state with a disposable device.” Thus, the above underlined portion of the amendment to claim 1 effectively changes the scope of the diagnostic product being marketed.

Applicant submitted that support for the amendment can be found in paragraph 0073 of the instant specification. Paragraph 0073 teaches that following data processing, pattern recognition tools can be utilized to identify subtle differences between phenotypic states. This portion of the specification does not teach different techniques of marketing diagnostic products wherein the products use representative patterns for a specific purpose of identifying a particular phenotypic state as opposed to a diagnostic that uses representative patterns in an unspecified manner. As such, this portion of the specification does not address the topic of marketing devices of different scope. Thus, the specification and claims as originally filed do not support the amendment to claim 1 for the reasons given above.

Step e) of amended claim 1 recites "selling said device", where said device refers to diagnostic products of previous step d) that use representative patterns "to identify a phenotypic state with a disposable device". The original wording of claim 1 did not read on a limitation regarding a disposable device used in identifying a phenotypic state or a limitation of selling said disposable device. Thus, the above underlined portion of the amendment to claim 1 adds the limitation of selling an unspecified disposable device.

Applicants submitted that support for the amendment can be found in paragraph 0024 of the instant specification. Paragraph 0024 teaches generically that revenue may be generated from the sale of disposable fluidics devices or disposable microfluidics devices. This portion of the specification does not teach the sale of a generic disposable device nor does it teach the sale of a disposable device that is used in conjunction with a diagnostic product that uses representative patterns in identifying a phenotypic state. As such, this portion of the specification does not address the limitation of selling an unspecified disposable device. Thus, the specification and claims as originally filed do not support the amendment to claim 1 for the reasons given above.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 5, 7-10, 14-20, 22-31, 38, 41, and 42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point

Art Unit: 1631

out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "said spectral components" in the third line of step b). There is insufficient antecedent basis for this limitation as the phrase "spectral components" is not previously recited in claim 1.

Claim 5, which depends from claim 3, recites the limitation "wherein said kits are FDA approved kits" in the first and second lines of the claim. There is insufficient antecedent basis for this limitation in the claim as the word "kits" is not previously recited in claim 3.

The term "common protein" in claim 28 is a relative term which renders the claim indefinite. The term "common protein" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. One interpretation of a "common protein" is a protein that is well known in the art to be expressed and associated with a particular condition such as a disease state. Another interpretation of a "common protein" is a protein wherein the polypeptide sequence that is composed of only the fundamental 20 amino acids. Yet another interpretation of a "common protein" is a protein that adopts a secondary and/or tertiary structure that has been previously identified and well characterized in the art. For the purposes of continuing examination, the Examiner has broadly construed the phrase "common protein" to mean any protein.

Art Unit: 1631

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 3, 7-10, 14-20, 22-24, 29-31, 38, and 42, rejected under 35

U.S.C. 102(a) as being clearly anticipated by Olek et al.

In regards to claims 1, 7-10, 15, 16, 22-24, 29-31, and 38, Olek et al. teaches collecting at least one biological sample derived from biological material of healthy and diseased individuals (specie of phenotypic state that is a disease diagnostic phenotype; collecting samples representing a clinical phenotypic state and samples representing patients without said phenotypic state; comprising the step of collecting samples in collaboration with a collaborator; wherein said collaborator is an academic collaborator; wherein said collaborator is a pharmaceutical company; wherein said pharmaceutical company collects said samples in a clinical trial). See Olek et al., paragraph 0066. Further, Olek et al. teaches repeating the method of the invention for at least 5 to 50 times (collecting more than 10 case samples; collecting more than 10 control samples; more than 50 of said case samples and 50 of said control samples are used; more than 100 of said case samples and 100 of said control samples are used). See Olek et al., paragraph 0085. Further, Olek et al. teaches determining relative amounts of protein relative to the expression level of at least one gene related to



Art Unit: 1631

a genetic disease phenotype by gel electrophoresis followed by mass spectrometry (specie of markers that are polypeptides; using electrophoresis followed by a mass spectrometry platform system to obtain mass spectral data in said case samples and in said control samples without regard to a specific identity of at least some of said spectral components). See Olek et al., paragraphs 0068, 0101, and 0102. Further, Olek et al. teaches an examples of the disclosed invention applied to prostate cancer wherein the results of the above analysis can be further used in diagnosis and/or therapy as a minimal set of reliable markers (identifying representative patterns of markers that distinguish datasets from case samples and control samples wherein said patterns contain more than 15 markers that are represented on output of said mass spectrometer, but the identity of at least some of said more than 15 markers is not known). See Olek et al. Paragraph 0104. Further, Olek et al. teaches that the disclosed invention has applications in the global analysis of cellular proteins which is a key area of research (marketing diagnostic products that use said representative patters to identify said phenotypic state). See Olek et al., paragraphs 0005 and 0006. Further, Olek et al. teaches the use of a Genomic Solutions Flexys robotic as well as computer-based analysis software, such as Imagemaster from Amersham-Pharmacia and "Z3" from Compugen, used in the diagnosis of prostate cancer, (cancer is described as a genetic disease, see Olek et al., paragraph 0023). These devices were obtained from the above mentioned companies and thus are clearly for sale, and are capable of being disposed of (with a disposable device, selling said disposable device; said diagnostic

Art Unit: 1631

products marketed by a diagnostic partner). See Olek et al, paragraphs 0101 and 0102.

In regards to claim 3, Olek et al. teaches the relevance of the disclosed invention is to genes with high overexpression or underexpression and provides support by reference to related work performed in a clinical laboratory (wherein said products are marketed in a clinical reference laboratory). See Olek et al., paragraphs 0009-0021.

In regards to claim 14, Olek et al. teaches a preferred method according to the invention wherein the sample selection is at least partially performed automatically by means of a computer device and such a device would be equipped to handle analysis (wherein data from one of said samples are being processed computationally while another of said samples are in said mass spectrometry platform). See Olek et al., paragraph 0073.

In regards to claims 17-20, Olek et al. teaches that gene panels, designated as a knowledge base or listing containing information about the selected genes under study such as the proteins and polypeptide sequences generated there from, are produced in the disclosed invention and that a preferred method according to the invention includes an analysis of at least 100 genes performed in parallel (wherein said patterns contain more than 30 polypeptide sequences that are represented on output of said mass spectrometer, but the identity of at least some of said more than 30 polypeptides is not known). See Olek et al. paragraphs 0061, 0068, 0070, and 0089.

Art Unit: 1631

In regards to claims 29 and 30, Olek et al. teaches "all currently known methods for the expression analysis of genes... can be used" and further cites mass spectrometry as a preferred analysis application (wherein said mass spectrometry platform is a time of flight spectrometer; wherein said mass spectrometry platform is a Hadamard mass spectrometer). See Olek et al., paragraph 0068.

In regards to claim 42, Olek et al. teaches a preferred method of the invention where the of said biological sample comprises isolating subcellular compartments, organelles, macromolecular structures and multiprotein complexes that can initially further limit the amount and complexity of the genes which take part in the inventive method (said samples contain complex mixtures of polypeptides). See Olek et al., paragraph 0067.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary.

Art Unit: 1631

Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3, 7-10, 14-20, 22-31, 38, 41 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olek et al. in view of Fouillet et al.

Olek et al. teaches a method wherein case samples and control samples regarding a clinical phenotype are collected, electrophoresis followed by a mass spectroscopy platform is used to obtain data on the samples, representative patterns are established from the datasets, and diagnostic products that use said patterns are marketed and devices sold. However, Olek et al. does not teach the a step of using a mass spectroscopy platform preceded by a step of preparing samples on a microfluidics device.

Fouillet et al. teaches that numerous sequence analysis of proteins is a laborious exercise, is commonly encountered in proteomics and related fields, and asserts that the disclosed invention drawn to microfluidic devices can remedy such experimental burdens. Further, Fouillet et al. teaches that the disclosed invention finds great applicability in proteomics and related fields as it facilitates better analysis of "disease specific proteins" that may serve as potential molecular markers. See Fouillet et al., paragraphs 0006, 0007, and 0351-0354.

Art Unit: 1631

In regards to claims 25, 27, and 28, Fouillet et al. teaches the methods and use of a microfluidics device for use in preparative and detection steps that encompass sample separation by means of electrophoresis (a step of preparing samples on a microfluidics device; said microfluidics device comprises a separations device; said microfluidics device removes high abundance proteins). See Fouillet et al., paragraphs 0160, 0300, and 0324.

In regards to claim 29, Fouillet et al. teaches that the microfluidics device is preferably semi-disposable and, in combination with a permanent device, is relatively inexpensive (diagnostic products are marketed with a disposable microfluidics device). See Fouillet et al., paragraph 0012.

In regards to claim 41, Fouillet et al. teaches that the disclosed microfluidics devices consist of microchannels instead of test tubes or microplates to carry out analyses and reactions and that the size of these channels are on the order of micrometers, while the reaction volumes are on the order of nanoliters or microliters. These dimension are on the order of the a delivery source for electrospray instrumentation (said microfluidics device comprises an electrospray source). See Fouillet et al., 0002.

Taken in view of Fouillet et al., it would be obvious to one of skill in the art to employ a microfluidics device in the manner described above prior to or at the time of electrophoresis and followed by use of a mass spectroscopy platform as taught by Olek et al. and previously described.

Art Unit: 1631

**Conclusion**

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Brennen et al. discloses integrated microfluidic related methodologies and systems pertinent to the invention of the instant application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. DeJong whose telephone number is (571) 272-6099. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D. can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

EDJ

  
ARDIN H. MARSCHEL  
PRIMARY EXAMINER